UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,569	10/11/2006	Alexander J. Pallenberg	600057.438USPC	2653

500 7590 03/18/2010

SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 5400
SEATTLE, WA 98104

EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
03/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,569	PALLENBERG ET AL.	
	Examiner	Art Unit	
	MAURY AUDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2009*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments are acknowledged. There are no amendments to the claims.

Election/Restrictions

As noted previously, Applicant's election without traverse of the following 3 species:

1) flourophore or photosensitizer (CHLORIN); bound to any agent that function as a

2) quenching agent (BETA CAROTENE/CAROTENOID); bound to any agent that can function as a

3) targeting moiety (ANTIBODY).

in the reply filed on 5/4/09 is acknowledged.

Claim Rejections - 35 USC § 103-Maintained

The rejection of claims 1-64 under 35 U.S.C. 103(a) as being unpatentable over Singh (20020197649), is maintained for the reasons of record. Applicant's arguments have been considered but are not found persuasive.

Applicant's primary argument, on page 14/16, para 2, of the response, is that:

> **"Applicants respectfully submit that while Singh may teach overlapping structural components of the claimed composition, one having skill in the art would recognize that the conjugates of Singh are not structurally identical and are functionally and mechanistically distinct from the presently claimed conjugates."** (Emphasis by underlining added by Examiner)

Independent claim 1, unamended, recites:

> 1. (Original) A conjugate, comprising: a fluorophore or a photosensitizer, a quenching agent; and a targeting moiety, wherein: the fluorophore or the photosensitizer is linked to the quenching agent and the targeting moiety in such a way that activation of the fluorophore or the photosensitizer is quenched until the targeting moiety is bound to a target, whereupon the quenching agent moves away from the photosensitizer, enabling activation of the photosensitizer upon irradiation with light of a suitable wavelength.

The claimed invention is a product. Arguments directed to function (2nd above, line 3) therefore are moot, absent something more. Thus, we are left with Applicant's assertion that the structures are not identical (1st above, line 3). The Examiner does not dispute this, hence the rejection was applied under 35 USC 103 Obviousness, as opposed to 35 USC 102, Anticipation.

Under the broadest reasonably interpretation of the claims, as Applicant himself admits in line 1-2, there is unequivocally "overlap" between the broadly claimed invention and the applied reference, Singh. Thus, it would have been predictable for one of ordinary skill in the art to arrive at the presently claimed product, as the rejection flushed out. **Absent evidence to the contrary OR AMENDMENT to positively claim a distinct combination of species that somehow produced unexpected results, beyond that which the skilled artisan would have expected by attaching the quenching agent (elected beta carotene/carotenoid) for Singh's identical purpose of optimizing the photosensitizer (elected chlorine) before activation, until the targeting moiety (elected any antibody) binds its target.**

Absent evidence to the contrary, the essential feature of the extremely open-ended claimed invention appears to be **attaching the quenching agent (elected beta carotene/carotenoid) for purpose of optimizing the photosensitizer (elected chlorine), which Singh recognizes.** The Examiner acknowledges Applicant's arguments that Singh requires at least two conjugates or separate molecules, but does not agree that this teaches away from the

essential feature of the claimed invention (until Applicant identifies what makes this open-ended product of combining virtually any of 3 known elements: flourophore/quenching agent/targeting moiety). Nothing would have prevented the skilled artisan from taking Singh and simply making only a single conjugate and still arrived at a more optimized photosensitizer upon target binding. Similarly, the Examiner is not convinced by Applicant's arguments that Singh only contemplates cleavage/release of the photosensitizer/flourophore. The photosensitizer still must carry out its function whether attached or not; otherwise what would be the purpose of Singh's use thereof? One of skill in the art would still recognize the essential parallel: that Singh - like Applicant- has attached the quenching agent to optimize the photosensitizer/flourophore – whether attached or not. Applicant has not provided any evidence that his product's photosensitizer/flourophore functions any differently/unexpectedly than Singh's.

For instance, did a SPECIFIC COMBINATION of the 3 elements of 1) quenching agent; 2) photosensitizer/flourophore; and 3) targeting moiety, evidence test results that optimized one or more of the agents v. a control when 1 or 2 of the other elements are not present with the 3rd?

Thus, as Applicant acknowledges, the "overlapping structural components" of the Singh product render Applicant's product, predictable; and therefore an obvious product in the eyes of the skilled artisan, until Applicant identifies and amends the claimed invention to embody some advancement over the art (e.g. unexpected result) he has created using these same "overlapping structural components".

The rejection is repeated below for continuity of record:

Singh teach the use of the same conjugates as presently claimed, including the option for the elected species thereof, for each of the 3 elements, AND the same rationale of using a quenching agent to optimize the photosensitizer before activation. See entire document, especially para's:

[0036] FIG. 2A illustrates another embodiment of the invention which uses antibodies as both the first and second binding agents. Analyte (200) is bound by first binding agent (204) having photosensitizer (PS.sub.1) and second binding agent (202) that has an electrophoretic tag consisting of a second photosensitizer (PS.sub.2) and mobility modifying moiety (M.sub.k). Second binding agent also has quencher (Q) adjacent to and quenching photosensitizer (PS.sub.2). Adjacent quencher (Q) prevents PS.sub.2 from being photoactivated to produce singlet oxygen, which in the unbound state (208) would result in self-cleavage and lead to spurious assay results. **That is, PS.sub.2 is in an inactive state when adjacent to the quencher. When within effective proximity (206) of PS.sub.1, cTag (212) is cleaved, after which it is separated and activated as shown in FIG. 1B.** FIG. 2B illustrates a similar assay configuration wherein the first (218) and second (224) binding agents are oligonucleotides. Another embodiment involving nucleic acid analytes and binding agents is illustrated in FIG. 2D. **Spurious activation of unbound photosensitizer (PS) is prevented by quencher (Q) which is held adjacent to photosensitizer (PS) by hairpin (252). When hairpin (252) hybridizes (256) to analyte (254) in a "taqman" type of assay, a polymerase (258) having 5'.fwdarw.3' exonuclease activity cleaves the cTag, which consists of photosensitizer (PS), mobility modifying moiety (M), and a portion of digested hairpin (252).** In accordance with such assay, the method provides: (a) contacting a sample comprising single-stranded nucleic acids (254) with an oligonucleotide (252) containing a sequence complementary to a region of the target nucleic acid and a labeled oligonucleotide containing a sequence complementary to a second region of the same target nucleic acid sequence strand, but not including the nucleic acid sequence defined by the first oligonucleotide, to create a mixture of duplexes during hybridization conditions, wherein the duplexes comprise the target nucleic acid annealed to the first oligonucleotide and to the labeled oligonucleotide such that the 3' end of the first oligonucleotide is upstream of the 5' end of the labeled oligonucleotide; (b) maintaining the mixture of step (a) with a template-dependent nucleic acid polymerase having a 5' to 3' nuclease activity under conditions sufficient to permit the 5' to 3' nuclease activity of the polymerase to cleave the annealed, labeled oligonucleotide and release cTags; and (c) detecting and/or measuring the released of cTags.

Detail Description Paragraph - DETX (44):
[0051] In one aspect, particularly when analytes are polynucleotides, a cleavage-inducing moiety may be an enzyme, such as cleavase, or a DNA polymerase with 5'.fwdarw.3' nuclease activity. In another aspect, particularly when analytes are proteins and binding agents are antibodies, a cleavage-inducing moiety is a group that produces an active species that is capable of cleaving a cleavable linkage, preferably by oxidation. Preferably, the active species is a chemical species that exhibits short-lived activity so that its cleavage-inducing effects are only in the proximity of the site of its generation. Either the active species is inherently short lived, so that it will not create significant background because beyond the proximity of its creation, or a scavenger is employed that efficiently scavenges the active species, so that it is not available to react with cleavable linkages beyond a short distance from the site of its generation. Illustrative active species include singlet oxygen, hydrogen peroxide, NADH, and hydroxyl radicals, phenoxy radical, superoxide, and the like. **Illustrative quenchers for active species** that cause oxidation include polyenes, **carotenoids**, vitamin E, vitamin C, amino acid-pyrrole N-conjugates of tyrosine, histidine, and glutathione, and the like, e.g. Beutner et al, Meth. Enzymol., 319: 226-241 (2000).

Detail Description Paragraph - DETX (75):
[0080] In the invention, photosensitizers are preferred as both cleavage-inducing moieties and signal amplification moieties. More preferably, a first photosensitizer acts as a cleavage-inducing moiety to release an electrophoretic tag that itself includes a second photosensitizer in inactivated form, **either being held adjacent to a quencher or being chemically inactive until an oxidizing reaction converts it into an active form.**

Table 1: Photosensitizer option as Chlorin.

It would have been obvious to one of ordinary skill in the art to have arrived at the present invention of products (conjugates) and methods of using said conjugate of:

1) flourophore or photosensitizer (CHLORIN); bound to any agent that function as a

2) quenching agent (BETA CAROTENE/CAROTENOID); bound to any agent that can function as a

3) targeting moiety (ANTIBODY);

in Singh, because Singh et al. advantageously teaches a conjugate that functions better when a quenching agent is attached to the photosensitizer, which is attached to an antibody; for the same purpose of Applicant's claimed invention of quenching the photosensitizer until the targeting moiety is bound to it's target, whereupon the effect natural/inherent physiological separation/moving away of the quenching agent from the photosensitizer, enabling activation of the photosensitizer upon irradiation with light of a suitable wavelength. And further expounds, like Applicant's myriad examples of each of the 3 conjugated elements each of the 3 elected compounds:

1) flourophore or photosensitizer (CHLORIN); bound to any agent that function as a

2) quenching agent (BETA CAROTENE/CAROTENOID); bound to any agent that can function as a

3) targeting moiety (ANTIBODY).

Singh teach that such conjugates may be used for known uses (e.g. assays, target-binding by antibody and known uses thereof in diagnostic/therapeutic effects) of said photosensitizer bound targeting moeities.

The judicious selection of the elected species would have been merely a matter of routine selection by one of ordinary skill in the art, based on Singh's express teaching and contemplation of each of the species within their respective genus.

Likewise, the judicious selection by the skilled artisan of means for binding the conjugate components and the addition of other agents with the conjugate would have been merely a matter of routine optimization, depending on the desired effect, absent evidence to the contrary of some unexpected result thereof – which was not found in the present description, as these are merely

ancillary aspects of the invention's intent, which Singh appears to hit on in the same fashion; namely the addition of a quenching agent to optimize photosensitizer results.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MA 3/13/10

/Maury Audet/
Primary Examiner, Art Unit 1654